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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/092,926	03/06/2002	Quan Nguyen	002558-064410US	1473

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EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/092,926	NGUYEN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *24-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/21/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-23 in the reply filed on January 1, 2005 is acknowledged. The traversal is on the ground(s) that despite the difference in literal claim scope, the overall concepts of the claims relate to a single invention-the use of mild denaturing conditions and reagents in the analysis of a sample of multiple proteins. Applicant argues that whether or not the claims can be separately classified, conducting a search of all claims together would enable Applicants to obtain a single patent on the invention and at the same time would not place an undue burden on the examiner. This is not found persuasive because restriction requirements are set forth for reasons of patentable distinction between each independent invention so as to warrant separate classification and search. The record set froth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other. The requirement is still deemed proper and is therefore made FINAL for reasons of record.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 the recitation "mild denaturation conditions" is vague and indefinite. It is unclear what is considered to be mild denaturation conditions. Is applicant referring to the addition of a denaturizing substance which is considered to be mild or is applicant referring to environmental conditions which are considered to be mild (for example, the temperature at which the method is performed) or is applicant referring to the combination of all parameters. Further, the term "mild" is a subjective term which renders the claim indefinite. Please clarify.

Claim 1, step (b) the recitation "the locus" there is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3-16 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al (US 2003/0153014) in view of Knowles et al (US 4,658,022).

Shen et al disclose methods for determining a plurality of modified proteins in a sample simultaneously. Shen et al disclose contacting the sample with a plurality of antibodies (first antibodies) immobilized on a solid support (page 2) in the form of an array (page 3, 16 and figures 1-2). Shen et al disclose performing wash steps to remove unbound materials from the first antibodies (p. 16, paragraph 0171). Shen et al disclose adding modification specific detection antibodies (second antibodies) to detect the modified proteins in the sample. Shen et al disclose that the modified proteins can be phosphorylated, (p. 2, paragraph 0016). Shen et al disclose the solid support can be sets of beads (particles) (p. 2, paragraph 0015). Shen et al disclose that the beads can be tagged. Shen et al disclose that the tag can be color, fluorescence, oligo, radiofrequency tage and other tag that can be easily used to separate beads with different tags (paragraph 0171). Shen et al disclose that the solid support can be made of glass or polystyrene (paragraph 0156). Shen et al disclose the solid support material

can be a slide or a chip (paragraph 0015). Shen et al disclose that the protein can be p38 MAP kinase. Shen et al disclose that the second antibodies can be biotinylated (paragraph 0171).

Shen et al differ from the instant invention in failing to teach contacting the sample under mild protein denaturation conditions with the first antibodies.

Knowles et al disclose methods for the detection of modified proteins. Knowles et al disclose contacting the sample to denaturing conditions with immobilized antibodies. Knowles et al disclose that the denaturing agent can be sodium dodecylsulfate (col. 8) (same agent applicant is using). Knowles et al disclose that denaturation effectively exposes or enhances the exposure of the linear peptide epitope or binding by the antibody reagent (abstract) and that it provides a general approach to improving the specificity of binding and detection of proteins of analytical interest such as in medical diagnostics (col 9, lines 20-24) and thus is particularly useful in performing immunoassays (abstract).

With respect to the recitation "mild" as recited in the claims. As stated above (see 112 2nd rejections) it is unclear what applicant intends and further since the combination of Knowles et al disclose the same denaturation agent (SDS) as applicant claims. Therefore, appears that the denaturing agent of Knowles et al is mild.

It would have been obvious to one of ordinary skill in the art to incorporate denaturation conditions and agents such as taught by Knowles et al into the method of Shen et al because Knowles et al teaches that denaturation effectively exposes or enhances the exposure of the linear peptide epitope or binding by the antibody reagent

(abstract) and that it provides a general approach to improving the specificity of binding and detection of proteins of analytical interest such as in medical diagnostics (col 9, lines 20-24) and thus is particularly useful in performing immunoassays.

8. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al and Knowles et al in view of Chin et al (US 6,197,599).

See above for teachings of Shen et al and Knowles et al.

Shen et al and Knowles et al differ from the instant invention in failing to teach wherein up to 100 modified proteins are detected.

Chin et al disclose arrays of immobilized antibodies for detecting analytes of interest. Chin et al disclose that the arrays can have thousands of different antibodies immobilized on a solid support (col 4). Chin et al disclose that this provides a powerful and quantitative tool for determining posttranslational modifications and provides a valuable tool to investigate protein and cellular regulations.

It would have been obvious to one of ordinary skill in the art to incorporate arrays as taught by Chin et al into the modified method of Shen et al because Chin et al teaches that this provides a powerful and quantitative tool for determining posttranslational modifications and provides a valuable tool to investigate protein and cellular regulations. Further, the number of 100 modified proteins as recited in the instant claims can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable

ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

9. Claims 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al in view of Knowles et al.

See above for teachings of Shen et al and Knowles et al.

Shen et al and Knowles et al differ from the instant invention in failing to teach contacting the product of step (c) with a labeled moiety.

Bayer et al., (Immunoassay, edited by Diamandis et al., The Avidin-Biotin System, Chapter 11, p. 237-267). Bayer et al disclose the use of the avidin-biotin system in immunoassay. Bayer et al disclose biotinylated antibodies which are detected by avidin-probe conjugates (labeled moiety) (p. 257-258). Bayer et al disclose several advantages of the avidin-biotin system. Bayer et al disclose that the avidin-biotin system greatly improves performance if the immunoassay and improves the characteristics of the capture system (p. 237) and that there is more control over the immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated (p. 255).

It would have been obvious to one of ordinary skill in the art to incorporate avidin-biotin system into the modified method of Shen et al because Shen et al specifically teaches that the second antibody can be biotinylated and further because Bayer et al

shows that this avidin-biotin system greatly improves performance if the immunoassay and improves the characteristics of the capture system and that there is more control over the immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated

10. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al and Knowles et al in view of Bayer et al as applied to claims 1, 3-17 and 20-23 above, and further in view of Roser (US 4,891,319).

See above for teachings of Shen et al., Knowles et al., and Bayer et al.

Shen et al., Knowles et al., and Bayer et al differ from the instant invention in failing to teach the labeled moiety comprises a phycoerythrin.

Roser teaches phycoerythrin Avidin/Streptavidin conjugate used in fluorescent assays (col 4, lines 43-54). Roser teaches that this fluorescent protein is 20 times brighter than fluorescein on a molar basis and can easily be coupled to probes.

It would have been obvious to incorporate phycoerythrin conjugates as taught by Roser into the modified method of Shen et al because Roser teaches that this fluorescent protein is 20 times brighter than fluorescein on a molar basis and can easily be coupled to probes.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
March 8, 2005

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03/09/05